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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,609	01/29/2004	Roberto Defez	6242CON	5195

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/767,609	DEFEZ ET AL.	
	Examiner	Art Unit	
	Michele K. Joike, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 January 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *PTO-948*.

DETAILED ACTION

Priority

It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/831,577 filed May 9, 2001. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such

prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Drawings

Drawings in the parent case, 09/831,577 were objected to based on the Draftperson's review (PTO-948), dated July 29, 2003. New corrected drawings were required in that application because of the reasons set forth in the attached Draftsperson's review (form PTO-948). The same drawings have been submitted in the current application and are also objected to based on the same reasons as set forth in the PTO-948 from application 09/831,577. New corrected drawings are required. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Figure 8 contains a nucleotide sequence that needs a sequence identifier.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claim 20 refers to plant biomass production that is at least 10%, which is not supported by the disclosure.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Specifically, the Abstract contains the improper legal language "said" in the second to last line of the Abstract. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection specifically addresses the written description issues regarding the promintron sequence to be used in the claimed invention.

Applicant claims the use of any promintron sequence homologous to that of SEQ ID NO: 1, or portion thereof, to induce the expression of any DNA sequence so as to significantly increase the biomass of any plant. The claims read on a broad genus of promintron sequences and portions thereof, and a broad genus of DNA sequences with the capacity to increase the biomass of any plant.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims homologous promintron sequences and portions of promintron sequences, as they relate to SEQ ID NO: 1, by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding the use of a single promintron sequence, SEQ ID NO: 1. The specification does not teach what fragments of this sequence would have the capacity to induce the expression of a DNA sequence such that it results in the increase of plant biomass, nor does the specification identify what portions of this sequence are required for its function as such. Furthermore, in the absence of such identifying characteristics, it would be impossible for the skilled artisan to envision what homologs of SEQ ID NO: 1 have the capacity to induce the expression of a DNA sequence in order to increase the biomass of a plant. Thus the skilled artisan could not envision what fragments of SEQ ID NO: 1 would be capable of inducing the expression of a gene, nor could the skilled artisan envision what homologs of SEQ ID NO: 1 would have this functional characteristic. Therefore, the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification sufficient to describe the claimed genus, because the specification only discloses a single embodiment, SEQ ID NO: 1, and provides no structure-function relationship for this sequence.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of homologs or portions of SEQ ID NO: 1 by disclosing structural or functional features of the

sequence so that one of skill in the art could envision the claimed invention. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of species of the claimed genus. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 19, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using SEQ ID NO: 1 to induce the expression of the *iaaM* and *tms2* genes to increase the biomass of a *Vicia hirsuta* plant, does not reasonably provide enablement for the use of any homolog or portion thereof.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention. The nature of the invention is a method of metabolic engineering, wherein a particular sequence (the promintron sequence) is used to induce the expression of a gene in a plant so that the biomass of the plant is increased relative to a plant wherein the expression of the gene is not induced by the promintron sequence. The invention involves effectively altering the metabolism of the plant so that its biomass is increased.

Scope of the invention. The scope of the invention is extremely broad on three fronts: (1) the sequence, a fragment or homolog of the described SEQ ID NO: 1, that can be used to induce the expression of a gene of interest; (2) the gene of interest that can be induced to result in an effective metabolic alteration in a plant so that the plant's biomass is increased significantly, relative to a plant where the gene is not induced; and (3) this can purportedly be done using any plant.

State of the art. The state of the art regarding the use of promintron sequences that are homologous or portions of SEQ ID NO: 1 to induce the expression of a gene of interest is silent. There is no description of SEQ ID NO: 1 in the prior art that would indicate what portions of the sequence would have the activity to induce the expression of a gene, nor is there a description of homologs of SEQ ID NO: 1 that would have this activity. The art is also silent on what genes can be induced to effectively alter the metabolism of a plant such that the biomass of any plant is increased. In fact, the prior art reflects the unpredictability of such "metabolic engineering" as a whole, suggesting that the use of any gene in any plant would be unpredictable in terms of increasing the biomass of that plant. A reference by Parekh *et al.* (*Appl. Microbiol. Biotechnol*: 287-301, 2000; see entire

reference) discusses the unpredictability that accompanies attempts at metabolic engineering. For example, Parekh states that metabolic engineering involves the empirical modification of metabolic pathways, most of which "are not readily controllable or measurable due to the nature of metabolic transients or reaction fluxes" (see for example the paragraph bridging pages 287 and 289). Furthermore, Parekh states that "with only limited knowledge of the physiology and genetics associated with the production of each molecule of interest, one is often led to an empirical approach to strain improvement", suggesting that the improvement of strains in terms of metabolic engineering is unpredictable, and relegated to a case-by-case basis. For example, the metabolic engineering of each type of plant would either require explicit knowledge of each particular plant or a specific example of the engineering of each particular plant in order to overcome the unpredictability of metabolically engineering each plant. Although this reference deals primarily with metabolic engineering as it concerns microorganisms, it is reflective of the unpredictability when practicing metabolic engineering in a more complex organism, such as a plant. This based on the rationale that metabolic engineering would not get any less complex as the organism that is being engineered becomes more complex. As a result of the lack of specific teachings regarding the metabolic engineering of plant cells to increase their biomass upon the induced expression of any gene, and the unpredictability associated with metabolic engineering as established by the Parekh reference, the skilled artisan would not be able to consult the prior art

when attempting to make and use the invention as claimed, and would be forced to consult the instant specification for guidance and working examples.

Number of working examples and Guidance provided by applicant. The instant specification provides only one example of a promintron sequence that is capable of inducing the expression of a gene to increase the biomass of a plant, SEQ ID NO: 1. As indicated in the rejection under Written Description, the specification does not identify functional portions of the promintron, so the skilled artisan would be unable to use homologs or portions of SEQ ID NO: 1 because the skilled artisan would not be able to envision these homologs or portions. Similarly, the specification only indicates that using SEQ ID NO: 1 to induce the expression of two specific genes, *iaaM* and *tms2*, results in an increase in plant biomass. Thus the instant specification only provides limited teachings on the metabolic engineering of plants to increase their biomass. Furthermore, the specification only exemplifies the expression of these two genes using SEQ ID NO: 1 in a single plant species, *Vicia hirsuta*. As a result, the skilled artisan would only be able to make and use the invention in terms of this particular embodiment, there being no alternate teachings to support to full scope of the claimed invention, in either the specification or the prior art.

Unpredictability of the art and Amount of experimentation required. The invention, as claimed in terms of its broad scope set forth above, is highly unpredictable. The skilled artisan would only be apprised of a single promintron sequence, SEQ ID NO: 1, which could be used to induce the expression of a gene for the purpose of increasing the biomass of a plant. In order to identify

portions or homologs of this sequence having the required function, the skilled artisan would be forced to practice undue trial and error experimentation first to identify the functionally relevant portions of SEQ ID NO: 1, being given no guidance as to what portions are functionally relevant. The skilled artisan would then have to identify homologs having these functionally relevant portions, and test them for their actual ability to induce the expression of a gene. Furthermore, the skilled artisan would have to practice unpredictable and undue trial and error experimentation to determine what genes would be able to affect the accumulation of plant biomass upon their induced experimentation. Finally, the skilled artisan would be required to determine the feasibility of this particular metabolic engineering event in all types of plants, including those that may not recognize the sequence of SEQ ID NO: 1 for promoter/enhancer activity (e.g., may not have the appropriate transcription factors) and those that may not have functional *iaaM* and *tms2* related pathways (e.g., downstream genes in the pathways to further metabolize the biochemical products obtained following expression of these genes). The unpredictability associated with this aspect of the invention is supported by the fact that metabolic engineering as a whole is unpredictable, that the instant specification only provides a single working example, and that there are literally millions of genes from different organisms that may or may not result in increased plant biomass upon their induced expression. Thus, the skilled artisan would be forced to undergo an enormous amount of experimentation to determine the enabled embodiments of the broadly claimed invention, especially in light of the guidance provided by the prior art and

the instant specification. As a result, the invention is not enabled for the full scope in which it is claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19, 20 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19, 20 and 22 provide for the use of a recombinant DNA molecule, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Furthermore, it is unclear as to whether or not the method is actually directed to the production of increased plant biomass or the induced expression of a gene, what steps are required to practice the invention, in what order the method steps must be performed in order to practice the method, or if the claims are indeed even directed to a method. For examination purposes, it is determined that the claims are drawn to a method of increasing the production of plant biomass by inducing the expression of a DNA sequence using the promintron sequence identified as SEQ ID NO: 1, or portions or homologs thereof.

Claims 19 and 22 do not conform to proper English grammar, and are therefore difficult to understand as a whole. For example, the claims read on "a

recombinant DNA molecule comprising a promintron sequence...said recombinant DNA molecule being covalently linked to the 3' end of said promintron sequence..."; it is unclear how the molecule can be attached to something that it comprises, unless it is attached to itself in a never-ending cyclical manner. Additionally, the claim recites "said recombinant DNA molecule being covalently linked to the 3' end of said promintron sequence, a DNA coding sequence..."; it is unclear if the promintron is a DNA coding sequence or if the DNA coding sequence refers to some other DNA coding sequence.

The term "significantly increase" in claims 19, 20 and 22 is a relative term that renders the claim indefinite. The term "significantly increase" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, the skilled artisan would not understand if a 1% increase was a significant increase or not, or if a 90% increase was required for the increase to be significant. As such, the metes and bounds of the claim are unknown, and therefore indefinite.

Claim 20 recites the limitation "said statistically significant increase" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19, 20 and 22 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER